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Spore forming bacteria infections and people who inject drugs: Implications for harm reduction

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ABSTRACT (Word count 310)

Background: There is no research on public health interventions that alert people who inject drugs (PWID) to clusters/outbreaks of severe bacterial infections. In Scotland, during the botulism cluster/outbreak of Dec 2014-July 2015 harm reduction (HR) messages detailed on a postcard (Botulism Postcard) were distributed to PWID between Feb-April 2015. We examined the impact of the Botulism Postcard on cluster/outbreak awareness, healthcare seeking and HR behaviours among PWID; and their views on such clusters/outbreaks.

Methods: The Botulism Postcard questionnaire survey was undertaken with 288 PWID recruited in Greater Glasgow and Clyde between May-August 2015. Multivariate logistic regression was undertaken. Between Oct 2015-January 2016 22 in-depth interviews were conducted with PWID in Glasgow and Edinburgh, these underwent thematic analysis.

Results: 38% (108/284) had never seen the postcard, 14% (40/284) had only seen it, 34% (98/284) read but not discussed it and 13% (38/284) had discussed it with service staff. Cluster/outbreak awareness was higher among those who had read (adjusted odds ratio (aOR) = 5.374, CI 2.394-11.349, $p<0.001$) or discussed the postcard (aOR = 25.114, CI 3.188-190.550, $p <0.001$); and symptom awareness was higher among those who had read (aOR = 2.664, CI 1.322-4.890, $p<0.001$) or discussed the postcard (aOR=6.707, CI 2.744-16.252, $p<0.001$) than among those who had never seen it. The odds of introducing HR was higher among those who had discussed the postcard (AOR= 3.304 CI 1.425-7.660, $p<0.01$) than

those who had only read it. PWID learnt about clusters/outbreaks from several sources and despite concerns they continued to inject during such events.

Conclusion: More widespread exposure to the Botulism Postcard during the outbreak/cluster was needed. The Botulism Postcard distributed to PWID may raise awareness of such events, the symptoms, and may encourage HR particularly when used as a tool by frontline staff to initiate discussion. Acknowledging that people continue to inject during clusters/outbreaks of such infections necessitates a pragmatic HR approach.

BACKGROUND

Since 2000, severe illnesses including botulism, tetanus and anthrax which are caused by spore forming bacteria (SFB) have emerged as a serious health problem among people who inject drugs (PWUD) across Europe (V. Hope et al., 2012; Palmateer et al., 2013). SFB produce hardy spores that are found to varying degrees in the environment, for example in soil. The spores can contaminate substances that they come in contact with, such as, illicit drugs. On entry into the body these spores can germinate and produce toxins that cause illness and can lead to death. Across six European countries there were an estimated 367 clinically or microbiologically confirmed cases of botulism, tetanus, anthrax and *Clostridium novyi* infection among PWID during 2000-2009 (V. Hope et al., 2012). Of these 367 cases, the UK reported 300 cases equating to an infection rate of approximately 2 infections per 1,000 PWID. Although the vast majority of SFB infections are associated with injecting drug use, the potential at-risk population for SFB infections is people who use drugs (PWUD) as there is a possibility that anthrax infection could also be acquired via the inhalation of drugs (Scottish Health Protection Network, 2017).

It is recognised that typical public health control measures, such as eradicating the contaminant at source or eliminating the contaminated source material, cannot be implemented during such outbreaks (National Anthrax Outbreak Control Team, 2011). This is because of the illicit nature of drug use and supply resulting in very limited intelligence on the whereabouts of the contaminated batches of drugs. Lessons learned from past clusters of illnesses due to SFB highlighted that rapid dissemination of risk communications to PWUD was a pertinent harm reduction (HR) measure (European Centre for Disease Prevention and Control, 2015; National Anthrax Outbreak Control Team, 2011).

The aim of risk communication during clusters/outbreaks is to alert PWUD to the ongoing event, to promote HR to reduce risk of exposure (for example, reduce heroin use or not to inject into the muscle or skin), promote symptom recognition and encourage timely healthcare seeking. There are no published studies that have examined the efficacy of such public health alerts for clusters/outbreaks of SFB and only a few studies have examined alerts in relation to other harms, such as alerts on heroin purity or drug adulteration following clusters of overdoses (Horyniak et al., 2010; Kerr, Small, Hyshka, Maher, & Shannon, 2013; Miller, 2007; Soukup-Baljak, Greer, Amlani, Sampson, & Buxton, 2015) or on changes in prescribed methadone dosages (Markwick, McNeil, Anderson, Small, & Kerr, 2016).

The two most recent large clusters/outbreaks of SFB experienced in Scotland were anthrax between December 2009-October 2010 with 14 deaths ((National Anthrax Outbreak Control Team, 2011), and wound botulism between December 2014-July 2015 involving 40 confirmed or probable cases and four deaths (NHS National Services Scotland, 2017). For both clusters, the likely source of contamination was heroin. With botulism, a contemporaneous outbreak occurred in Norway which may suggest a common contaminated batch of heroin ((European Centre for Disease Prevention and Control, 2015).

During the Scottish botulism cluster/outbreak, risk communication with PWID was facilitated by a Botulism Postcard designed by NHS Greater Glasgow & Clyde (NHS GGC) and Scottish Drugs Forum (see Figure 1). This was widely distributed to PWID via injecting equipment provision (IEP) services operating from pharmacies and drug treatment services within the NHS GGC area. The Botulism Postcard recommended PWID seek immediate medical advice for the named symptoms and to introduce the following HR: reduce or eliminate heroin use, switch from injecting to smoking heroin, and not to inject into muscles

or skin. The highest risk for botulism is among PWID who intentionally/accidentally inject intramuscularly or subcutaneously as botulism spores require an anaerobic environment, such as damaged muscle or skin, for growth (European Centre for Disease Prevention and Control, 2015).

[Figure 1 IN HERE Colour not required for figure.].

This paper addresses the gap in evidence on the effectiveness of risk communication aimed at alerting PWID to outbreaks of bacterial infections. To the best of our knowledge, this is the first paper to assess a public health intervention during a SFB cluster/outbreak, and to examine PWID views on such clusters/outbreaks. The intervention under evaluation was the Botulism Postcard distributed to PWID. We drew upon data from two separate but concurrent studies, namely: the Botulism Postcard questionnaire survey and qualitative interviews which examined PWID views and experiences of skin and soft tissue infections (SSTI). The Botulism Postcard questionnaire survey was used to examine the level of exposure to the postcard and its association with cluster/outbreak awareness, knowledge of signs and symptoms, healthcare seeking and HR behaviours. These main findings were supplemented with in-depth interview data on PWID views of the anthrax and botulism clusters/outbreaks taken from a wider study on PWID views and experiences of (SSTI). Those experiencing SFB infections associated with injecting may present with SSTI alongside other symptoms. The botulism symptoms are listed in Table 3.

METHODS

i) Quantitative study

The quantitative data were derived from the February 2015-March 2016 data collection sweep of Scotland's national survey of PWID, the Needle Exchange Surveillance Initiative (NESI). NESI is a cross sectional, voluntary, anonymous and confidential survey which has been on-going since 2008 (University of the West of Scotland, Health Protection Scotland, Glasgow Caledonian University, & West of Scotland Specialist Virology Centre, 2015). The Botulism Postcard questionnaire was distributed to PWID only in NHS GGC during May to August 2015 as an additional insert to the NESI questionnaire. Data collection focussed on the NHS GGC only as it appeared to have been the focus of the outbreak with the majority of cases either residing in, or having sourced their drugs from Glasgow (NHS National Services Scotland, 2017). The Botulism Postcard questionnaire was initially piloted in NHS GGC resulting in minor changes to the wording. Only a subset of the NHS GGC sample were able to complete the additional Botulism Postcard questionnaire as NESI data collection had already started within NHS GGC in February 2015. A team of trained interviewers asked eligible participants to take part in the NESI survey. Those eligible to participate were those who had ever injected drugs and had not already participated in the current data collection sweep. The exclusion criteria included those who appeared intoxicated at the time of the interview. Interviews lasted around 20 minutes and were conducted in a private room at each site; informed consent was provided by all participants. Participants were offered a £5 shopping voucher after completion of the interview. If any participant indicated they had never seen the Botulism Postcard they were provided with a copy at the end of the interview. Approval for the original NESI study was obtained from the West of Scotland NHS Research Ethics Committee and Caldicott approval was granted from NHS GGC for the Botulism Postcard questionnaire survey.

i) The intervention and intervention measure

A total of 4,000 Botulism Postcards were initially distributed to all 69 IEP sites in NHS GGC, and a further 3,000 were distributed to those sites which needed their supplies replenished. The Botulism Postcard was offered to clients using any IEP service between Feb-April 2015. The postcard was intended as a tool for IEP staff to engage PWID in discussion on botulism key facts and safer injecting advice (as illustrated on the postcard in Figure 1). The postcard was accompanied by training resources for IEP staff to support the delivery of the messages, and ensure staff were able to answer any questions from PWID in relation to the outbreak. The level of exposure to the Botulism Postcard (Botulism Postcard I) was derived from a number of survey questions to give four mutually exclusive levels: Never seen; seen but not read; read but not discussed; and discussed (with a member of staff with or without reading). Staff were those working in IEP services. Those who had only seen the postcard were considered to have been exposed to the postcard as it was available to them within the services even though they chose not to read it. For some of the analysis presented in Table 1, Botulism Postcard I was recoded to give two values 'never seen or only seen' and 'read or discussed' (Botulism Postcard II) to accommodate the lower sample size for the analysis with 'Seek help at A&E'. Botulism Postcard II was also used for the bi-variate analysis examining the demographic differences by exposure to the postcard for ease of presentation in Table 1, whilst Botulism Postcard I was used within the logistic regression.

Outcome measures

Four outcomes were examined including: i) awareness of the botulism cluster/outbreak (No/Yes) which was measured by asking 'Within the past six months have you heard about botulism among people who inject drugs?' ('cluster/outbreak awareness'); ii) symptom awareness (No/Yes) which was measured by asking 'Do you know of any of the symptoms of

botulism?' and whether correctly named symptoms were given to the question 'Can you tell me any of the symptoms?' ('symptom awareness'); iii) would help be sought from accident and emergency (A&E) (No/Yes) for the named symptoms was derived from the question 'If you had any of these symptoms would you seek help?' and 'Where would you go?' ('seek help from A&E') and iv) change in injecting behaviours (No/Yes) was derived from 'As a result of reading [the postcard], have you changed the way you inject?' and 'As a result of discussing [the postcard], have you changed the way you inject?' ('injecting behaviour changes'). Only those participants who had either read or discussed the postcard were asked about their injecting behaviour change.

Statistical Analysis

Descriptive statistics was used to describe the sample. Pearson's $\chi 2$ test was used to examine bivariate associations between participant demographics including their HR uptake and exposure to postcard (Botulism Postcard II), 'cluster/outbreak awareness', 'symptom awareness', 'injecting behaviour change' and 'seek help from A&E' (Table 1). Sample sizes may be less than the total of 288 participants due to missing data. Pearson's $\chi 2$ test and Mann-Whitney was used to examine differences in participant demographic and HR uptake by whether or not had completed the Botulism Postcard questionnaire. Holms Sequential Bonferroni correction was used for post-hoc comparisons for significant Pearson's $\chi 2$ test. Multivariable logistic regression was used to calculate the odds of i) 'cluster/outbreak awareness', ii) 'symptom awareness' and iii) 'injecting behaviour change' with the level of Botulism Postcard exposure (Botulism Postcard I) (Table 2). For the first two of the regression models the reference category for Botulism Postcard I was 'never seen' and for the third, which examined 'injecting behaviour changes', the reference category was 'read' as only those PWID who had read or discussed the postcard were asked about injecting

behaviour changes. Potential confounders selected for inclusion in the multivariable logistic regression were those variables found to be statistically significant ($p<0.05$) using the bivariate analysis in Table 1 and included: excessive weekly alcohol intake, time since onset of injecting, prison status, had a SSTI, gender, homelessness in past six months and combined needle/syringe and opiate substitution treatment (N/S-OST) uptake. Regression was generated by forward step-wise analysis and was statistically significant at $p<0.05$. All analyses were undertaken with SPSS version 22.

ii) Qualitative study

Supplementary interview data relating to PWID views of SFB clusters/outbreaks was drawn from a larger qualitative study, which examined views and experiences of SSTI, led by the lead author (KD). In-depth interviews were conducted by KD with 22 PWID recruited from a pharmacy IEP service in NHS GGC and a drug treatment service in NHS Lothian between October 2015-January 2016. These areas were selected because both have experienced recent but different clusters/outbreaks of bacterial infections: for NHS GGC this was the botulism cluster/outbreak whilst in NHS Lothian ethylphenidate, a new psychoactive substance, was implicated in a Group A Streptococcus cluster/outbreak during 2014-2105. Heroin was the predominant drug injected in both NHS GGC and NHS Lothian during 2015 and 2016 (NHS GGC 92%, NHS Lothian 90%) but there were some local variations in the drugs injected, for example, with new psychoactive substances injecting more prevalent in NHS Lothian (24% versus 9% in NHS GGC((NHS Health Protection Scotland, 2017). Staff at the recruitment sites directed PWID to KD who explained the purpose of the study and checked eligibility criteria. The inclusion criteria was to have injected at least once in the past six months, to have had an injecting related SSTI (defined as an abscess, cellulitis or necrotising fasciitis) in the past year and to be 18 years or older. Those younger than 18 years, or older than 65 years

were excluded. The interviews lasted between 21 and 67 minutes, were audio recorded and conducted in a private room at the recruitment sites. Informed consent was taken prior to interview, participants were assured of confidentiality and were given pseudonyms. The interviews were transcribed verbatim by a transcriber who had signed a confidentiality agreement. Participants were offered a £25 shopping voucher at the end of the interview. Ethical approval for the qualitative study was obtained from NHS West of Scotland Research Ethics Committee and University of the West of Scotland Ethics Committee. Framework analysis, which is a matrix based method used to code the interview data into themes and sub-themes, was used to thematically categorise the interviews (Ritchie, Lewis, McNaughton Nicholls, & Ormston, 2014). The main domains covered in the interviews included PWID experiences and views of SSTI; how PWID responded to their SSTI infection with respect to self-treating, seeking healthcare and HR; and their views on recent SFB clusters/outbreaks. The latter domain only is presented in this paper. Descriptive statistics were used to describe the qualitative sample. It was not established whether any of the qualitative sample had also participated in the Botulism Postcard questionnaire survey.

RESULTS

i) Quantitative study: Botulism Postcard

399 participants completed the additional Botulism Postcard Questionnaire out of a total of 992 participants interviewed during the NESI data collection sweep in NHS GGC area. Of these 399 participants, 33 duplicate responses from individuals who had completed the questionnaire more than once were excluded (this includes 3 respondents with insufficient identifiers for duplicate identification), 52 who had not injected in the past 6 months and 26 who had not injected heroin were also excluded as all reported cases of botulism had used heroin (NHS National Services Scotland, 2017). Data from the remaining 288 participants were analysed.

There were difference in demographics between those who completed the Botulism Postcard questionnaire and those who had not: those who had completed it were on average older by two and a half years than those who had not (completed: median = 40.5, IQR = 10.35; not completed: median = 37.53, IQR = 9.33; M-W = 45095.500, p=0.000, n=699) and had been injecting for on average two and a half years longer than those who had not (completed: median = 16.42, IQR = 12.33; not completed: median = 14.02, IQR=12.27; M-W = 49279.500, p=0.000, n=695).

Of the sample who had completed the Botulism Postcard questionnaire, 74% (212/285) were male, 30% (86/288) were 45 years plus, 24% (70/287) had been homeless in the past six months, 51% (148/287) had been injecting for 16 years plus and 79% (228/288) were currently prescribed methadone.

Just over a third of respondents had never seen the postcard (38%, 108/284), 14% (40/284) had seen but not read it, 34% (98/284) had read it without discussion with IEP service staff and 13% (38/284) had discussed it, of which four had not read it. Table 1 shows that those who had 'high N/S-no OST' uptake (where high N/S is defined as 200%+, that is, at least twice as many N/S as injections but not currently on OST) were least likely to have read or discussed the postcard (14%, 3/22) (CHI=13.43, df=3, p=0.004). Only three of these 22 with 'high N/S-no OST' had solely relied on secondary distribution for their N/S supplies suggesting the group mainly attended IEP services.

Approximately three out of four PWID had heard of the botulism cluster/outbreak (76%, 219/288), 33% (95/288) had correctly named symptoms and of those who correctly named symptoms, 97% (88/91) would hypothetically seek help if they had symptoms. Of those 88 participants who would seek help, 79% (70/88) would seek help from A&E (as instructed on the postcard), 26% (23/88) from a general practitioner/family doctor, 9% (8/88) from a drug service, 1% (1/88) from a needle exchange, 2% (2/88) from NHS 24, and none would seek help from a pharmacy or hostel/homeless service. Of those PWID who had experienced a previous SSTI, the majority of those who had sought help at A&E for their most recent SSTI would also seek help at A&E for botulism symptoms (87%, 26/30) compared to 67% (10/15) of those who had not previously sought help at A&E for SSTI. A total of 29% (40/136) had changed their injecting behaviour (introduced HR) either as a result of reading or discussing the postcard; however, of the whole sample this represents 14% (40/288) of PWID.

[TABLE 1 in here]

Table 2 presents the multivariable analysis. We undertook three multivariable logistic regressions with 'cluster/outbreak awareness', 'symptom awareness' and 'injecting behaviour change' as the dependent variable (or outcome) and exposure to the Botulism Postcard (Botulism Postcard) as the independent variable (or intervention). Multivariable analysis demonstrates that those who had read the postcard and those who had discussed the postcard had higher odds of 'cluster/outbreak awareness' and 'symptom awareness' compared to those who had never seen the postcard; and those who had discussed the postcard had higher odds of changing their injecting behaviour compared to those who had read the postcard.

[Table 2 in here]

Table 2 shows the non-intervention variables that were also associated with our outcome measures in the multivariable regression analysis. Those who had an excessive weekly alcohol consumption (that is, > 14units per week for women and >21units per week for men) had lower odds of being aware of both botulism and its symptoms; those injecting for 16 plus years had higher odds of being aware of botulism; and those who had been in prison during the previous six months had lower odds of symptom awareness; and those homeless in the past six months were more likely to have introduced harm reduction related injecting behaviour change.

Table 3 shows 'inflammation at the injection site' was the most commonly named symptom. The definition of inflammation was undefined. Of all those who had seen the postcard (with or without reading it or discussing it), Table 3 shows that 71% (128/179) had seen it in the needle exchange and 39% (70/179) in a drug treatment service. Of those who had a discussion with staff, these were mainly with drug treatment staff (68%, 25/37) rather than

pharmacy staff (30%, 11/37). Of those who had read the postcard, 22% (22/98) had changed their injecting behaviour (introduced HR) and of those who had a discussion, 47% (18/38) had changed their injecting behaviour (introduced HR). The main change made from reading the postcard was 'made sure injected into a vein', while the changes resulting from discussion were varied as shown in Table 3.

[Table 3 in here]

ii) Qualitative study: PWID views on botulism and anthrax clusters/outbreaks

The qualitative study sample included 14 and eight participants interviewed in the NHS Lothian and NHS GCC respectively. The sample was composed of 68% male, had an average age of 36.50 years (median = 36.50, IQR=9) and had been injecting on average for 15.5 years (median =15.5, IQR=13.5). All participants had injected heroin in the past 6 months, and heroin was the main drug injected by 82% (18/22) of participants. During the qualitative interviews participants were asked about their thoughts on the recent Scottish clusters/outbreaks of anthrax (2009-2010) and botulism (2014-2015).

Some remembered seeing or hearing the warnings about the anthrax and/or botulism clusters/outbreaks either from alerts displayed in pharmacies or drug treatment centres, newspaper reporting or knowing people who had experienced a SFB infection or hearing about people dying.

> *Interviewer:* There was the botulism as well.
> Respondent: Yeah. Aye.
> *Interviewer:* Do you remember them?
> Respondent: I've seen the leaflets still. They're still up in some places.
> *Interviewer:* Right. Okay.
> Respondent: Exchanges and things like that. (Patricia, Female, 34 years old)

Interviewer: Do you remember the anthrax?
Respondent: Ma pal had it. (Tanya, Female, 21 years old)

Concern was expressed for both the botulism and the anthrax outbreaks. Paul who heard about the botulism from alerts in a drug treatment centre noted a general level of concern:

> Respondent: It was a lot of talk about it, the botulism. A lot of people were a bit scared, you know? It's botulism, know? Wee bit weary about it, you know what I mean?
> *Interviewer: Mmhm.*
> Respondent: 'Cause they didnae know how they were catching it, you know what I mean? (Paul, Male, 42 years old)

Despite such concern, our participants did or would still inject during a SFB outbreak because of their drug dependency:

> "But like the anthrax, that was scary eh. You were always like, 'oh imagine if it, what's wrong wi' this or what's in this bit'. But you still take it. If you're a user and you've got a habit you dinnae really care eh until it happens. ……" (Caroline, Female, 27 year old)

Or they continued to inject because they trusted their dealers:

> *Interviewer:* Aye. Aye. Aye. Did that stop you at all? What did you think? See when you heard that [anthrax and botulism] was going round, what did you think?
> Respondent: Thought 'I wouldnae like that.' Do you know what I mean? But it's the chance you take every time you inject, do you know that? …
> *Interviewer:* Yeah... So, you didn't stop or it didn't change anything?
> Respondent: No. 'Cause I thought the people I get my drugs fae wouldnae get it. And they didnae, thank God (Brian, 42 years old, Male).

DISCUSSION

This is the first paper to examine the impact of a public health information HR intervention, in the form of a postcard, which was distributed via IEP sites to PWID in response to the emergence of a botulism cluster. The Botulism Postcard may have improved awareness of the cluster/outbreak, symptoms and encouraged HR; this may have been maximised when the card was used as a trigger by IEP staff for discussion. However, further mechanisms are

needed to increase the level of exposure to the postcard in order to maximise its potential as an effective public health intervention.

Notably, just under 40% of the respondents reported not seeing the postcard – this may in part reflect frequency of attendance at IEP sites: those with 'high N/S but no OST' uptake were most likely not to have seen it – this may indicate that some collected ample N/S supplies infrequently, for example, a box of 100 N/S at one IEP visit, while OST necessitates daily or more frequent visits thereby increasing the likelihood of seeing the postcard. However, these non-frequent attenders were only one small group and there is a need to improve exposure to the postcard in general to ensure more are seeing, reading and discussing it. Other methods or venues to engage PWID with public health alerts are needed. Notably, although approximately 40% of PWID had never seen the postcard, the level of cluster/outbreak awareness among this group was still high at 60% but symptom awareness was somewhat lower at 30%. Their cluster/outbreak awareness may have been raised from other potential sources as suggested by our qualitative data which showed newspaper reporting, word of mouth from knowing people who had experienced a SFB infection or hearing about people dying were also sources of information.

The botulism outbreak received some, albeit limited, mainstream media reporting (Anon, 2015; BBC, 2015; Musson, 2015). Work in Canada concerned with communication about drug quality issues (Soukup-Baljak et al., 2015) noted that PWUD felt multiple sources of information, such as peers, fliers or posters, newspaper, television, Internet and social media be used for alerts. Appropriately designed date stamped fliers displayed throughout the community including alleyways, IEP services and supervised injecting facilities are helpful alerts, but they should be removed after a period of time so that PWID are not de-sensitised to future alerts (Soukup-Baljak et al., 2015). In addition, peer-delivered public health warnings may be an under-utilised approach for disseminating drug warnings and health

communications (Markwick et al., 2016); building relationships between health service providers and peers may help the reach of public health alerts (Soukup-Baljak et al., 2015) and opportunities to initiate discussion between PWID and frontline service staff about injecting risk factors can be valued by both PWID and staff (Horyniak et al., 2010). Possible reasons why a limited number of the PWID (14%) in our study had not read the postcard despite seeing it may include literacy issues. This may suggest a need for more graphics, or some PWID considered it irrelevant because of a perceived existing awareness or knowledge but notably this was not borne out for symptom awareness. Only 13% of all PWID were engaged in a discussion with staff. These discussions were more likely to be had with staff in drug treatment services rather than in pharmacies – suggesting the drug treatment service setting was more conducive, offered more opportunity to engage with PWID or these staff were more comfortable engaging with PWID. The barriers to engaging PWID in discussion need to be identified.

The majority of all PWID had heard of the botulism cluster/outbreak, approximately a third of all PWID correctly named symptoms but only a minority of all PWID (14%) had introduced HR. Multivariable logistic regression analysis showed that the odds of cluster/outbreak and symptom awareness were higher among those PWID who had read the postcard and was highest among those who had discussed the postcard with IEP staff than those who had never seen the postcard. And those who had a discussion had higher odds of having introduced HR than those who had read it. This suggests the postcard was beneficial, however given the cross sectional nature of this study we cannot assume causality and need to be mindful that some PWID may have read or discussed the postcard because of an existing awareness or interest. Discussion with IEP staff would seem to have been particularly effective. This may be because discussion allows for tailored or detailed advice thereby allowing for a more persuasive argument to bring about improved awareness and HR,

and/or it highlights a level of trust between the PWID and IEP staff (Treloar, Rance, Yates, & Mao, 2016)). Simultaneously raising awareness and understanding of these clusters/outbreaks among frontline staff dealing with PWID, which was an intervention also implemented (NHS National Services Scotland, 2017), maybe an equally important public health intervention.

Approximately a third of PWID who had read or discussed the postcard had self-reported changing their injecting behaviour (introducing HR). Of the specified HR advice provided on the postcard, the advice most heeded was to 'made sure injected into a vein'. This advice is pertinent as the bacterium does not grow in blood (European Centre for Disease Prevention and Control, 2015) – and may have been the most heeded as it offers pragmatic advice which recognises that PWID will continue to inject during SFB clusters/outbreaks as highlighted in our qualitative data. PWID are appreciative of pragmatic injecting advice (Harris & Rhodes, 2012)). Notably, some of the other injecting changes mentioned by our PWID in our quantitative survey were not specified on the postcard but still constituted general HR, for example, using sterile N/S. But other changes would be ineffective during a botulism cluster/outbreak, for example, burning the drug solution for longer. Our qualitative data demonstrated a misplaced level of trust in dealers as batches of heroin cannot be identified as being contaminated with SFB without microbiological analysis.

It is less clear whether the postcard would promote healthcare seeking at A&E but nevertheless many of our respondents with symptom awareness would hypothetically seek help from A&E for botulism symptoms. This may be because the postcard highlighted the potential seriousness of a botulism infection or that PWID typically seek healthcare for SSTI at A&E anyway; the majority of those who had sought healthcare for a previous SSTI would do the same for botulism and 'inflammation at injection site' was the most commonly named botulism symptom. But, we need to be aware that the PWID self-reported intention to seek help for botulism symptoms may not reflect actuality. Although PWID typically attend A&E

for SSTI they can delay seeking this healthcare typically for 5 days (V. Hope, Ncube, Parry, & Hickman, 2015), consequently one of the purposes of the postcard was to promote timely healthcare seeking.

As well as the risk communication delivered by the Botulism Postcard other HR interventions have been recommended by public health guidance to address SFB infections among PWUD (Scottish Health Protection Network, 2017). These include IEP and OST. It is further recommended that OST provision should be enhanced by reducing/removing waiting lists and/or reviewing eligibility criteria for receiving/remaining on OST for the duration of an outbreak/cluster.

Other strategies such as drug checking services, opiate assisted treatment (including prescription heroin) and supervised consumption facilities have been suggested to manage overdose risks associated with fentanyl adulterated heroin or ecstasy (Fairbairn, Coffin, & Walley, 2017; Saleemi, Pennybaker, Wooldridge, & Johnson, 2017; Thomson, Lampkin, Maynard, Karamouzian, & Jozaghi, 2017). Drug checking services which have been offered to ecstasy and stimulant users (Saleemi et al., 2017) may be less feasible for SFB contaminated heroin. SFB contaminated heroin is not distinguishable from uncontaminated heroin without microbiological testing and the laboratory techniques required would not provide the immediate results needed to inform a drugs user's intention to use as demonstrated by drug checking services at music festivals. In addition, microbiological testing may not be able to confirm the presence of bacterial species in surrendered or seized heroin linked to an outbreak/cluster (McLauchlin et al., 2002). The proposed opening of a supervised injection facility and provision of heroin assisted treatment within Glasgow in response to the HIV, botulism and anthrax outbreaks, and drug related deaths ((Tweed & Rodgers, 2016) may ensure that further HR responses for future SFB outbreaks be offered. Access to prescription heroin ensures an unadulterated source of heroin and the presence of

medical services within a supervised injection facility may aid the detection of SFB infections and promote prompt healthcare seeking.

Non-intervention variables were also found to be associated with cluster/outbreak and symptom awareness and the introduction of HR in the multivariable analysis. Those with excessive alcohol intake had lower odds of awareness for both the cluster/outbreak and its symptoms; this suggests this group may need to be targeted with further interventions to increase awareness or retention of information. Those who had been in prison the previous six months had lower odds of symptom awareness – this suggests that those in prison may have been aware of the cluster/outbreak in general via the media reporting but this did not alert them to the symptoms. Consequently, upon prison release during a cluster/outbreak PWID may need to be given a postcard. Those who were homeless in the past six months had increased odds of introducing HR related injecting behaviours. This may suggest that some of the HR specified on the card was most relevant to their circumstances, for example, public injecting environments including cold and dark alleyways/stairwells cause PWID to struggle to inject into veins – making the advice to inject into veins more pertinent. Equally, the homeless may also have been exposed to outreach HR services, such as Assertive Outreach, which may have encouraged HR behaviours.

This study has a number of limitations. Although one of the strengths of the Botulism Postcard questionnaire survey was its inclusion as part of the NESI survey which coincided with the unanticipated botulism cluster/outbreak in NHS GGC, we were unable to include all NHS GGC NESI participants. The NESI data collection had already started prior to the preparation of the Botulism Postcard questionnaire survey. The Botulism Postcard questionnaire survey sub-sample was older and had been injecting longer than the NESI sample, and so our findings should be generalised with some caution. Quantitative data was not collected on other factors which may influence awareness or HR, such as, exposure to

media reporting and social/peer networks. Botulism cluster/outbreaks are unpredictable and need a prompt response, and because of resource constraints, a full scale, multi-faceted evaluation was not feasible. However, we supplemented our main quantitative study with data from a concurrent but separate qualitative study to help strengthen our findings. Although the qualitative interviews allowed for a more contextualised understanding of PWID views, they cannot be generalised nor quantified. Despite these limitations, this study is unique and provided an assessment of a public health intervention during an unanticipated cluster/outbreak of SFB. The findings are of interest to services across Europe who have previously dealt with such clusters/outbreaks of bacterial infections or who will deal with future clusters/outbreaks.

To conclude, a postcard distributed via IEP services to alert PWID to clusters/outbreaks of SFB infections demonstrated the potential for raising awareness of clusters, symptoms, and encouraging HR, particularly when used by IEP staff to facilitate discussion with PWID. However, further work is needed on identifying effective mechanisms for wider distribution and engagement with PWID during clusters/outbreaks. Our findings reiterate the importance of providing PWID with pragmatic injecting advice and HR as they will continue to inject during clusters/outbreaks despite awareness and concerns. Distribution of the postcard in response to future clusters/outbreaks may need to include targeted activities for PWID leaving prison and those with excessive alcohol intake. Future qualitative research is needed with PWID to explore their views on, and perceived impact of, postcard interventions on their injecting and HR. The views of frontline IEP staff on the implementation of such interventions also is needed to identify best practice and barriers.

Authors' contributions

AT, AM, SH, NP and DG designed the NESI survey. AM, KD, KR, AT developed the Botulism Postcard questionnaire. GP, JC, EH, DL developed and implemented the intervention. AM, TK and AT led on the implementation of the NESI survey. KD undertook data analysis. KD, VH, KR and AT designed the qualitative study. KD implemented and analysed the qualitative interviews. KD wrote the drafts of the manuscript. All authors critically reviewed and approved the final manuscript.

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Conflict of interests:

JC received professional fees from Indovior to address a scientific meeting and has received funding from Frontier Medical for educational support and conference attendance. All other authors report no potential conflicts.

Figure 1: The Botulism Postcard (double-sided) distributed by harm reduction services during the December 2014-June 2015 wound botulism cluster/outbreak.

Table 1. Demographics of PWID by exposure to postcard, cluster/outbreak awareness, symptom awareness, changed injecting behaviour and would seek help at A&E.

		Botulism Postcard II		Cluster/Outbreak Awareness		Symptom Awareness		Changed injecting behaviour [a]			Would seek help at A&E [b]		
Demographic/HR uptake	N	Yes n %	P-value	Yes n %	P-value	Yes n %	P-value	N	Yes n %	P-value	N	Yes n %	P-value
Male	212	100 (47)	0.604	159 (75)	0.596	67 (32)	0.399	100	28 (28)	0.842	63	48 (76)	0.870
Female	73	37 (51)		57 (78)		27 (37)		37	11 (30)		27	21 (78)	
Ever homeless													
No	81	44 (54)	0.211	63 (78)	0.651	28 (35)	0.681	44	7 (16)	0.03	27	20 (74)	0.703
Yes	206	95 (46)		155 (75)		66 (32)		95	32 (34)		63	49 (78)	
Homeless in past 6 months													
No	217	110 (51)	0.113	168 (77)	0.308	69 (32)	0.544	110	25 (23)	0.006	67	53 (79)	0.351
Yes	70	29 (41)		50 (71)		25 (36)		29	14 (48)		23	16 (70)	
Ever in prison													
No	89	48 (54)	0.227	70 (79)	0.488	31 (35)	0.656	48	10 (21)	0.143	30	23 (77)	0.968
Yes	199	92 (46)		149 (75)		64 (32)		92	30 (33)		61	47 (77)	
Prison status													
Never	89	48 (54)	0.259	70 (79)	0.15	31 (35)	0.004	48	10 (21)	0.115	30	23 (77)	[c]
In the past (not 6 months)	161	76 (78)		125 (78)		58 (36)		76	24 (32)		56	44 (79)	
Past 6 months	32	12 (37)		20 (62)		2 (6)		12	6 (50)		2	- (0)	
Age (years)													
<= 35	62	33 (53)	0.758	47 (76)	0.05	23 (37)	0.639	33	13 (39)	0.051	21	16 (76)	[c]
36-39	71	36 (51)		51 (72)		26 (37)		36	11 (31)		25	19 (76)	
40-44	69	31 (45)		47 (68)		20 (29)		31	11 (35)		19	15 (79)	
>45	86	40 (46)		74 (86)		26 (30)		40	5 (12)		26	20 (77)	
Excessive alcohol [d]													
No	216	109 (50)	0.345	172 (80)	0.01	82 (38)	0.004	109	32 (29)	0.649	79	61 (77)	0.714 [e]
Yes	64	28 (44)		41 (64)		12 (18)		28	7 (25)		11	8 (73)	
N/S-OST Coverage [f, g]													
Low N/S no OST	38	19 (50)	0.004	33 (87)	0.093	34 (13)	0.681	19	10 (53)	0.07	12	8 (68)	[c]
Low N/S and OST	157	86 (55)		122 (78)		35 (55)		86	22 (26)		53	42 (79)	
High N/S no OST	22	3 (14)		13 (59)		23 (5)		3	-		5	4 (80)	
High N/S and OST	68	31 (46)		50 (73)		31 (21)		31	8 (26)		20	15 (75)	

Table 1 (Contd). Demographics of PWID by exposure to postcard, botulism awareness, symptom awareness, changed injecting behaviour and would seek help at A&E.

		Botulism Postcard II		Cluster/Outbreak Awareness		Symptom Awareness		Changed injecting behaviour [a]			Would seek help at A&E [b]		
Demographic/HR uptake	N	Yes n %	P-value	Yes n %	P-value	Yes n %	P-value	N	Yes n %	P-value	N	Yes n %	P-value
OST status													
Never	13	3 (23)	0.062	6 (46)	0.014	1 (8)	0.133	3	2 (67)	0.110	1	- (0)	[c]
Currently	228	118 (52)		173 (76)		77 (34)		118	30 (25)		74	58 (78)	
In the past	47	19 (40)		40 (85)		17 (36)		19	8 (42)		16	12 (75)	
N/S Coverage [f, h]													
< 100%	97	53 (55)	0.041	72 (74)	0.049	31 (32)	0.419	53	11 (21)	0.063	29	21 (72)	0.739
100-199%	83	52 (53)		83 (85)		37 (38)		52	21 (40)		36	29 (81)	
≥ 200%	63	34 (38)		63 (70)		26 (29)		34	8 (23)		25	19 (76)	
Time since onset injecting (yrs.)													
< 5	43	17 (40)	0.453	29 (67)	0.048	14 (33)	0.944	17	8 (47)	0.039	14	11 (79)	[c]
6–10	33	18 (55)		23 (70)		12 (36)		18	8 (44)		12	9 (75)	
11-15	63	34 (54)		44 (70)		22 (35)		34	5 (15)		20	15 (75)	
16+	148	71 (48)		123 (83)		47 (32)		71	19 (27)		45	35 (78)	
Had a SSTI													
Never	135	65 (48)	0.665	94 (70)	0.047	40 (30)	0.022	65	18 (28)	0.04	38	28 (74)	0.798
In the past (not last year)	95	50 (53)		77 (81)		28 (29)		50	10 (20)		27	21 (78)	
In the past year	55	25 (45)		46 (84)		27 (49)		25	12 (48)		26	21 (81)	
Botulism Postcard I										0.004			
Never seen	108			65 (60)	0.000	22 (30)	0.000	-	-				
Seen but not read	40			26 (65)		2 (10)		-	-				
Read but not discussed	98			87 (89)		44 (45)		98	22 (22)				
Discussed [i]	38			37 (97)		24 (63)		38	18 (47)				
Botulism Postcard II [j]													
Never seen or seen not read											26	17 (65)	0.098
Read or discussed [i]											65	53 (81)	

a. Includes only those who had read and/or discussed the postcard.

b. Did not seek help at A&E Includes 3 participants who would not seek help from any source. This is a hypothetical question.

c. > 20% of cells have expected count less than 5

d. Defined as > 14units/week for women and >21units per week for men

e. Fischers Exact Test

f. Includes N/S obtained from others and is adjusted for number of months injecting

g. ‘Low N/S no OST’ is < 200% N/S and no OST; ‘Low N/S and OST’ is < 200% N/S and currently on OST; ‘High N/S no OST’ is ≥200% N/S and no OST; ‘High N/S and OST’ is ≥200% N/S and currently on OST

h. <100%=does not have a sterile N/S for every injection, 100-199%=has between one and just less than 2 N/S per injection; ≥200%=has 2 plus N/S per injection

i. Discussed with member of staff at the pharmacy needle exchange or drug treatment service. 4 of the 38 who had discussed had not read the postcard

j. Botulism Postcard recoded to Postcard II accommodate lower sample size for analysis with ‘Seek help at A&E’

Table 2. Univariable and multivariable models of association between awareness of the botulism cluster, its symptoms and injecting behaviour change by exposure to the postcard

Outcome		Univariable			Multivariable [a, b]		
		OR	(95% CI)	P-value	AOR	(95% CI)	P-value
Cluster/outbreak awareness	Botulism Postcard I						
	Never seen	1			1		
	Seen but not read	1.229	(0.577-2.616)	0.593	1.432	(0.595-3.448)	0.423
	Read but not discussed	5.232	(2.506-10.923)	0.000	5.213	(2.394-11.349)	0.000
	Discussed	24.477	(3.236-185.124)	0.002	24.646	(3.188-190.550)	0.002
	Alcohol excessive						
	No	1			1		
	Yes	0.456	(0.248-0.838)	0.011	0.422	(0.205-0.868)	0.019
	Time since onset inject						
	< 5 years	1			1		
	6–10 years	1.110	(0.417-2.955)	0.834	0.714	(0.232-2.191)	0.556
	11-15 years	1.118	(0.485-2.575)	0.793	0.921	(0.345-2.462)	0.870
	16+ years	2.375	(1.101-5.126)	0.028	2.236	(0.919-5.439)	0.078
Symptom awareness	Botulism Postcard I						
	Never seen	1			1		
	Seen but not read	0.434	(0.140-1.350)	0.150	0.419	(0.131-1.347)	0.145
	Read but not discussed	3.185	(1.723-5.889)	0.000	2.543	(1.322-4.890)	0.005
	Discussed	6.701	(2.985-15.042)	0.000	6.678	(2.744-16.252)	0.000
	Alcohol excessive						
	No	1			1		
	Yes	0.377	(0.190-0.748)	0.005	0.327	(0.148-0.724)	0.006
	Prison						
	Never	1			1		
	In the past (not 6 mon)	1.054	(0.613-1.811)	0.850	1.105	(0.598-2.042)	0.750
	Past 6 months	0.125	(0.028-0.557)	0.006	0.106	(0.022-0.515)	0.005
Injecting behaviour change	Botulism Postcard I						
	Read	1			1		
	Discussed	3.109	(1.405-6.879)	0.005	3.304	(1.425-7.660)	0.005
	Homeless past 6 months						
	No	1			1		
	Yes	3.173	(1.351-7.454)	0.008	2.841	(1.148-7.031)	0.024

a. Multivariable models adjusted for excessive weekly alcohol intake, time since onset of injecting, prison status, had a SSTI, gender, homelessness in past six months and combined NS-OST uptake

b. Prison status, had a SSTI, OST status, gender, homelessness in past six months and combined NS-OST uptake did not load into Cluster/outbreak model; time since onset of injecting, had a SSTI, OST status, gender, homelessness in past six months and combined NS-OST uptake did not load into Symptom model; Excessive weekly alcohol intake, time since onset of injecting, prison status, had a SSTI, combined needle/syringe and opiate substitution treatment (N/S-OST) uptake, gender did not load into 'Injecting behaviour change' model

Table 3. Symptoms named, where postcard was seen and discussed, and injecting behaviour changes made after reading or discussing the Botulism Postcard.

	n (%)
Symptoms named (N=288)	
Blurred or double vision	34 (12)
Slurred speech, difficultly speaking	23 (8)
Difficulty swallowing	19 (7)
Difficulty with longue/lip movements	6 (2)
Drooping or falling of eyelids	9 (3)
Extreme weakness	14 (5)
Inflammation at injection site	57 (20)
Paralysis of arm and legs	13 (4)
Difficulty breathing	18 (6)
Where seen the Botulism Postcard [a] (N=179)	
At needle exchange	128 (71)
At drug treatment centre	70 (39)
Friend/family	1 (< 1)
Other:	
General Practitioner/Health Centre	9 (5)
Sheriff Court/Prison/Social Work	4 (2)
Hostel	2 (1)
Everywhere	2 (1)
Changed the way you inject as a result of reading the Botulism Postcard [b] (N=136)	37(27)
Change made: (N=36) [c]	
Reduced heroin	5 (14)
Stopped heroin	2 (6)
Made sure injected into a vein	10 (28)
Stopped skin/muscle popping	5 (14)
Used foil for smoking heroin	4 (11)
Other:	
Use sterile or clean IE	5 (14)
Generally more careful	4 (11)
Dealer/supply/drug [d]	4 (11)
Drug preparation [e]	1 (3)
Clean injecting site	1 (3)
Stopped sharing	1 (3)
Discussed the Botulism Postcard with staff (N-38):	
Where from (N=37)[f]	
Drug treatment service	25 (68)
Needle exchange	11 (30)
Both	1 (3)
Changed the way you inject as a result of discussing the Botulism Postcard (N=37) [f]	14 (38)
Change made: (N=13) [g]	
Reduced heroin	2 (15)
Stopped heroin	2 (15)
Made sure injected into a vein	2 (15)
Stopped skin/muscle popping	1 (8)
Used foil for smoking heroin	2 (15)
Other:	
Being more careful	3 (23)
Stopped injecting	2 (15)
Dealer/drug supply [h]	2 (15)
Stopped sharing	1 (8)

a. This includes all those who had seen the Botulism Postcard
b. This includes all those who had read the Botulism Postcard
c. There was one case of missing data so N is not 37
d. Includes the following responses: Careful about where obtaining drugs from, got heroin believed to be safe, try to find out about purity, would n't use if heroin looked different
e. Includes the following responses: Burn it longer.
f. There was one case of missing data so N is not 38
g. There was one case of missing data so N is not 14
h. Includes the following responses: Changed supplier, use own stuff

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